Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. (ORIGINAL) Use of a phosphodiesterase antagonist to reduce insulin resistance in a mammalian patient suffering therefrom.

2. (ORIGINAL) Use of a phosphodiesterase antagonist in the manufacture of a medicament useful in reducing insulin resistance in a patient suffering therefrom.

3. (ORIGINAL) Use of a phosphodiesterase antagonist in the manufacture of a medicament useful in amplifying the effect of nitric oxide on skeletal muscle insulin-mediated glucose uptake in a mammalian patient.

4. (CURRENTLY AMENDED) Use of claim 1, ~~2 or 3~~ wherein the insulin resistance is hepatic insulin sensitizing substance-dependent insulin resistance ("HDIR").

5. (CURRENTLY AMENDED) Use of claim 1, ~~2, 3 or 4~~ wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol, caffeine, milrinone, amrinone pimobendan, cilostamide, enoximone, teroximone, vesmarinone, rolipram and R020-1724.

6. (CURRENTLY AMENDED) Use of claim 1, ~~2, 3 or 4~~ wherein the phosphodiesterase antagonist is an antagonist of at least one phosphodiesterase of subtype 3 and 5.

7. (ORIGINAL) Use of claim 5 wherein the antagonist is zaprinast.

8. (ORIGINAL) Use of claim 5 wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol and caffeine.

9. (CURRENTLY AMENDED) Use of ~~any preceding~~ claim 1 wherein the patient is a human.

10. (ORIGINAL) A pharmaceutical composition comprising a phosphodiesterase antagonist and at least one other drug used in the treatment of diabetes.

11. (ORIGINAL) The pharmaceutical composition of claim 10 further including a pharmaceutically acceptable liver-targeting substance.

12. (CURRENTLY AMENDED) The composition of claim 10 ~~or 11~~ wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol, caffeine, milrinone, amrinone pimobendan, cilostamide, enoximone, teroximone, vesmarinone, rolipram and R020-1724.

13. (ORIGINAL) The composition of claim 12 wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol and caffeine.

14. (CURRENTLY AMENDED) The composition of claim ~~9 or~~ 10 wherein the phosphodiesterase antagonist is an antagonist of at least one of phosphodiesterase of subtype 3 and 5.

15. (CURRENTLY AMENDED) The composition of claim 10, ~~11, 12, 13 or 14~~ wherein the other drug is at least one of insulin, insulin analogues, sulfonylurea agents, tolbutamide, acetohexamide, tolazamide, chlorpropamide, glyburide, glipizide, glimepiride, biguanide agents, metformin, alpha-glucosidase inhibitors, acarbose, miglitol, thiazolidinedione agents (insulin sensitizers), rosiglitazone, pioglitazone, troglitazone, meglitinide agents,

repaglinide, cholinesterase inhibitors, donepezil, tacrine, edrophonium, demecarium, pyridostigmine, phospholine, metrifonate, neostigmine, galanthamine, zanapezil, cholinergic agonists, acetylcholine, methacholine, bethanechol, carbachol, pilocarpine hydrochloride, nitric oxide donors, products or processes to increase NO synthesis in the liver (increasing NO synthase activity), SIN-1, molsidamine, N-acetylcysteine, cysteine esters, L-2-oxothiazolidine-4-carboxolate (OTC), gamma glutamylcystein and its ethyl ester, glutathione ethyl ester, glutathione isopropyl ester, lipoic acid, cysteine, cystine, methionine, S-adenosylmethionine, products or processes to reduce the rate of NO degradation in the liver, products or processes to provide exogenous NO or an exogenous carrier or precursor which is taken up and releases NO in the liver, antioxidants, vitamin E, vitamin C, 3-morpholinosyndnonimine, glutathione increasing compounds, N-acetylcysteine, cysteine esters, L-2-oxothiazolidine-4-carboxolate (OTC), gamma glutamylcystein and its ethyl ester, glutathione ethyl ester, glutathione isopropyl ester, lipoic acid, cysteine, cystine, methionine, and S-adenosylmethionine.

16. (ORIGINAL) The composition of claim 11 wherein the liver-targeting substance is at least one of bile salts, albumin and liposomes.

17. (ORIGINAL) A kit comprising:

a phosphodiesterase antagonist in a pharmaceutically acceptable carrier; and

instructions for the administration of the phosphodiesterase antagonist to reduce insulin resistance in a mammalian patient.

18. (ORIGINAL) The kit of claim 17 further comprising means to administer the phosphodiesterase antagonist.

19. (ORIGINAL) A method of reducing insulin resistance in a mammalian patient comprising administering a suitable phosphodiesterase antagonist.

20. (ORIGINAL) The method of claim 19 wherein the insulin resistance is HISS-dependent insulin resistance.

21. (ORIGINAL) A method of amplifying the effect of nitric oxide on skeletal muscle insulin sensitivity comprising administering a phosphodiesterase antagonist.

22. (ORIGINAL) A method of increasing glucose uptake by skeletal muscle of a patient, comprising administering a phosphodiesterase antagonist.

23. (CURRENTLY AMENDED) The method of one of claims 19, ~~20, 21 or 22~~ wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol, caffeine, milrinone, amrinone pimobendan, cilostamide, enoximone, teroximone, vesmarinone, rolipram and R020-1724.

24. (ORIGINAL) The method of claim 23 wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol and caffeine.

25. (CURRENTLY AMENDED) The method of any one of claims 19, ~~20, 21, 22 or 23~~ wherein the phosphodiesterase antagonist is an antagonist of at least one of phosphodiesterase of subtype 3 and 5.

26. (CURRENTLY AMENDED) The method of ~~any preceding~~ claim 1 further comprising administering at least one other drug used in the treatment of diabetes.

27. (ORIGINAL) The method of claim 26 wherein the other drug is at least one of insulin, insulin analogues, sulfonylurea agents, tolbutamide, acetohexamide, tolazamide, chlorpropamide, glyburide, glipizide, glimepiride, biguanide agents, metformin, alpha-glucosidase inhibitors, acarbose, miglitol, thiazolidinedione agents (insulin sensitizers), rosiglitazone, pioglitazone, troglitazone, meglitinide agents, repaglinide, cholinesterase inhibitors, donepezil, tacrine, edrophonium, demecarium, pyridostigmine, phospholine, metrifonate, neostigmine, galanthamine, zanapezil, cholinergic agonists, acetylcholine, methacholine, bethanechol, carbachol, pilocarpine hydrochloride, nitric oxide donors, products

or processes to increase NO synthesis in the liver (increasing NO synthase activity), SIN-1, molsidamine, N-acetylcysteine, cysteine esters, L-2-oxothiazolidine-4-carboxolate (OTC), gamma glutamylcystein and its ethyl ester, glutathione ethyl ester, glutathione isopropyl ester, lipoic acid, cysteine, cystine, methionine, S-adenosylmethionine, products or processes to reduce the rate of NO degradation in the liver, products or processes to provide exogenous NO or an exogenous carrier or precursor which is taken up and releases NO in the liver, antioxidants, vitamin E, vitamin C, 3-morpholinosyndnonimine, glutathione increasing compounds, N-acetylcysteine, cysteine esters, L-2-oxothiazolidine-4-carboxolate (OTC), gamma glutamylcystein and its ethyl ester, glutathione ethyl ester, glutathione isopropyl ester, lipoic acid, cysteine, cystine, methionine, and S-adenosylmethionine.

28. (CURRENTLY AMENDED) The method of ~~any preceding~~ claim 1 wherein the phosphodiesterase antagonist is preferentially targeted to the liver.

29. (ORIGINAL) The method of claim 28 wherein the phosphodiesterase antagonist is targeted to the liver using albumin.

30. (ORIGINAL) The method of claim 28 wherein the phosphodiesterase antagonist is targeted to the liver using a plurality of liposomes.

31. (ORIGINAL) The method of claim 28 wherein the phosphodiesterase antagonist is targeted to the liver using bile salts.

32. (CURRENTLY AMENDED) The method of claim 19, ~~20, 21, 22 or 23~~ wherein the phosphodiesterase antagonist is administered by intravenous administration.

33. (CURRENTLY AMENDED) The method of claim 19, ~~20, 21, 22 or 23~~ wherein the phosphodiesterase antagonist is administered by transdermal administration.

34. (CURRENTLY AMENDED) The method of claim 19, ~~20, 21, 22 or 23~~ wherein the phosphodiesterase antagonist is administered by oral administration.

35. (CURRENTLY AMENDED) The method of claim 19, ~~20, 21, 22 or 23~~ wherein the phosphodiesterase antagonist is administered by intra peritoneal administration.

36. (CURRENTLY AMENDED) The method of claim 19, ~~20, 21, 22 or 23~~ wherein the phosphodiesterase antagonist is administered by portal vein injection.

37. (CURRENTLY AMENDED) The method of claim 19, ~~20, 21, 22 or 23~~ wherein the phosphodiesterase antagonist is administered orally at a dose of between about 2 and 300 mg/kg body weight.

38. (CURRENTLY AMENDED) The method of claim 19, ~~20, 21, 22 or 23~~ wherein the phosphodiesterase antagonist is administered intravenously at a dose of between about 5 and 500 μg/kg body weight.

39. (CURRENTLY AMENDED) The method of ~~any preceding~~ claim 1 wherein the patient suffers from at least one of: chronic liver disease, chronic hypertension, type II diabetes, fetal alcohol syndrome, gestational diabetes, obesity, age-related insulin resistance, and hepatic nerve damage.

40. (CURRENTLY AMENDED) The method of ~~any preceding~~ claim 1 wherein the patient is a human.

41. (NEW) Use of claim 2 wherein the insulin resistance is hepatic insulin sensitizing substance-dependent insulin resistance ("HDIR").

42. (NEW) Use of claim 3 wherein the insulin resistance is hepatic insulin sensitizing substance-dependent insulin resistance ("HDIR").

43. (NEW) Use of claim 2 wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol, caffeine, milrinone, amrinone pimobendan, cilostamide, enoximone, teroximone, vesmarinone, rolipram and R020-1724.

44 (NEW) Use of claim 3 wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol, caffeine, milrinone, amrinone pimobendan, cilostamide, enoximone, teroximone, vesmarinone, rolipram and R020-1724.

45. (NEW) Use of claim 2 wherein the phosphodiesterase antagonist is an antagonist of at least one phosphodiesterase of subtype 3 and 5.

46. (NEW) Use of claim 3 wherein the phosphodiesterase antagonist is an antagonist of at least one phosphodiesterase of subtype 3 and 5.

47. (NEW) The method of one of claims 21 wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol, caffeine, milrinone, amrinone pimobendan, cilostamide, enoximone, teroximone, vesmarinone, rolipram and R020-1724.

48. (NEW) The method of one of claims 22 wherein the antagonist is at least one of vinpocetine, zaprinast and dipyridamole, sildenafil, theophylline, aminophylline, isobutylmethyl xanthine anagrelide, tadalafil, dyphylline, vardenafil, cilostazol, caffeine, milrinone, amrinone pimobendan, cilostamide, enoximone, teroximone, vesmarinone, rolipram and R020-1724.

49. (NEW) The method of any one of claims 21, wherein the phosphodiesterase antagonist is an antagonist of at least one of phosphodiesterase of subtype 3 and 5.

50. (NEW) The method of any one of claims 22, wherein the phosphodiesterase antagonist is an antagonist of at least one of phosphodiesterase of subtype 3 and 5.

51. (NEW) The method of claim 21, wherein the phosphodiesterase antagonist is administered by intravenous administration.

52. (NEW) The method of claim 22, wherein the phosphodiesterase antagonist is administered by intravenous administration.

53 (NEW) The method of claim 21, wherein the phosphodiesterase antagonist is administered by transdermal administration.

54. (NEW) The method of claim 22, wherein the phosphodiesterase antagonist is administered by transdermal administration.

55. (NEW) The method of claim 21, wherein the phosphodiesterase antagonist is administered by transdermal administration.

56. (NEW) The method of claim 22, wherein the phosphodiesterase antagonist is administered by transdermal administration.

57. (NEW) The method of claim 21, wherein the phosphodiesterase antagonist is administered by intra peritoneal administration.

58. (NEW) The method of claim 22, wherein the phosphodiesterase antagonist is administered by intra peritoneal administration.

59. (NEW) The method of claim 21, wherein the phosphodiesterase antagonist is administered by portal vein injection.

60. (NEW) The method of claim 22, wherein the phosphodiesterase antagonist is administered by portal vein injection.

61. (NEW) The method of claim 21, wherein the phosphodiesterase antagonist is administered orally at a dose of between about 2 and 300 mg/kg body weight.

62. (NEW) The method of claim 22, wherein the phosphodiesterase antagonist is administered orally at a dose of between about 2 and 300 mg/kg body weight.

63. (NEW) The method of claim 21, wherein the phosphodiesterase antagonist is administered intravenously at a dose of between about 5 and 500 μg/kg body weight.

64. (NEW) The method of claim 22, wherein the phosphodiesterase antagonist is administered intravenously at a dose of between about 5 and 500 μg/kg body weight.